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ORIGINAL MEMOIRS.

ACID INTOXICATION: ITS SIGNIFICANCE IN SURGICAL CONDITIONS.

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THE condition of acid intoxication observed in surgical cases has been brought forcibly to our notice, during the past year, by a series of cases occurring at the Boston Children's Hospital and Boston City Hospital. In the present article I wish to call attention to those occurring at the latter hospital during my service as house surgeon. I am indebted to the members of the surgical staff, in whose services these cases were observed, for their kind permission in allowing me to report this series.

In a review of the literature of the subject I find series of cases reported by various writers which I feel sure are identical with those I am about to report. While they have been reported under other headings, they have been practically identical in clinical signs and results with those observed at the Boston City Hospital, and, while the mortality in the latter series has not been so great, there is no doubt but that they represent but one disease. While I do not pretend to explain the cause of the condition found in these cases, I feel sure that by presenting this series, I will contribute to a subject which will eventually receive most careful attention in medical as well as in surgical cases, and perhaps stimulate to some extent physiological, clinical, and pathological investigation in this most interesting subject.

While not claiming that the term acid intoxication definitely describes the condition present, I feel that it will serve until the etiology of this puzzling disease has been definitely determined. Under this term are to be included all those cases which have been reported under the headings of Acetonuria, Acetonæmia, and Aciduria. In presenting this series there has occurred some clinical evidence of the existence of a form of acid intoxication which is apparently due to some disturbance in the body metabolism, and all the cases present in the urine acetone and diacetic acid, either separately or together.

This report is based upon the observation of about 400 surgical cases during a period of four months. The urine of these cases was examined (1) immediately upon entrance to the hospital; (2) within twelve to forty-eight hours after the administration of a general anæsthetic; (3) if at any subsequent time clinical signs suggested this condition, or the urine showed the presence of acetone or diacetic acid; and (4) the urine was examined in most cases every other day until the clinical symptoms had ceased and the urine no longer contained a pathological amount of acetone or diacetic acid. Of the 400 cases observed, symptoms of acid intoxication were present in forty-six. In some of these grave symptoms were present; in others, excepting a slight odor to the breath, there was nothing clinically to suggest this condition, and in several acetone and diacetic acid was only discovered in the urine by routine examination on entrance.

History.—The importance of this acid intoxication, produced in the organism by some metabolic change, has been recognized by a study of the intoxication occurring in diabetes mellitus. The coma found in this condition was thought to be due to the presence of acetone in the blood, and that the latter was never found excepting in diabetes. Of late years, however, it has been shown that acetonuria occurs in conditions independent of diabetes, and that the presence of acetone and diacetic acid is probably a manifestation of the intoxication due to various fatty acids following some pathological change in metabolism.

Acetone was first recognized as a pathological constituent of the urine in connection with diabetes, by Petters, in 1857. In the same year Kaulish reported a series of cases of diabetes in which he found acetone present in the urine of a number of cases, and considered the occurrence of coma to be due to acetonæmia. This theory was disputed by Kussmaul in 1874, who doubted the toxic action of acetone to be the cause of diabetic coma. At a later period Gerhardt and others demonstrated conclusively that acetone was associated with diacetic acid and β-oxybutyric acid in the urine and blood of diabetic patients.

It has long been recognized that diabetic patients are poor subjects for anæsthesia, especially when their urine contains acetone. Becker, in 1894, reported three fatalities following anæsthesia in diabetic patients, in which acetonuria was present at the time of the operation. He considered that death was due in these cases to some cause common with the production of acetonuria, and later he examined the literature and found twelve cases in which death resulted in diabetic patients, following anæsthesia. He was led to believe, therefore, that diabetic patients, although showing no clinical symptoms of a grave condition previous to operation, were liable, owing to some change in the process of metabolism, to pass into a condition of coma and death. Brewer, in 1902, reported a fatal case of appendicitis in which he ascribed the cause of death as due to acetonæmia. Guthrie, in 1903, reported a series of cases in which death occurred following the administration of chloroform in children, in which autopsy showed the condition of fatty liver to be present. While he did not suspect the presence of acetone and diacetic acid in the urine, his description of the cases showed a set of clinical symptoms similar to those about to be described in the present article. Brackett, Stone, and Law, in July, 1904, in a report from the Boston Children's

Hospital, under the title of "Aciduria associated with Death after Anæsthesia," presented a series of fourteen cases in which death was undoubtedly due in the five fatal cases to an acid intoxication. From this list of clinical evidence of the presence of a, so far undetermined, cause in some cases of death, it can readily be seen that at times there exists a condition, not always recognized, that will have great weight in estimating the degree of a favorable prognosis in surgical cases. This condition of acid intoxication was formerly thought to occur only in fatal cases of diabetes; but late researches, including those cited above, prove conclusively that the condition is entirely independent of diabetes, and moreover that acid intoxication should be considered as a distinct lesion.

As all the cases in the literature of the subject have been presented under the term of acetonuria, and as this condition is present only as a symptom of acid intoxication, it will be used for the time being as synonymous with the latter condition.

An excess of acetone and diacetic acid in the urine has been recognized in the following diseases: (1) in the late stages of diabetes mellitus; (2) in starvation; (3) in malignant growths; (4) in digestive disturbances; (5) in septic processes, general or local; (6) in infectious fevers; (7) in pregnancy, associated with a dead fœtus; (8) in certain psychoses; (9) in autointoxications; (10) in chronic morphinism; (11) in phosphorous poisoning; (12) following general anæsthesia; (13) in injuries to the cerebrospinal system; (14) in shock due to injury; (15) in cases associated with fatty liver, and (16) probably in cases of uræmia. It has been produced experimentally by the administration of phlorizin, and by extirpation of the pancreas and solar plexus.

The presence of acetone (0.02 gramme in fifty ounces) as a normal constituent of the urine has been proven by physiologists. It is also excreted by the lungs and a very small amount is contained in the fæces. (Schwarz, L. Müller.) The amount of acetone in the urine may be increased by the administration of oleic acid, as shown by Joslin. He administered to a patient 100 grammes of oleic acid, and found that in the twenty-four hours there were excreted 1700 milligrammes of acetone.

That the amount of acetone excreted is no indication of the severity of the acid intoxication present is shown by Brackett, Stone, and Law in the series of cases reported from the Boston Children's Hospital. In one of their fatal cases the total excretion of acetone in the twenty-four hours was approximately 142 milligrammes; and, while it is considerably more than normal, cases of diabetes have been reported in which the daily excretion of acetone was 100,000 milligrammes.

Acetone was considered by Kussmaul to be the toxic agent; but from the foregoing statement of Brackett, Stone, and Law, and from the fact that acetone has been found in the blood in large amounts, and has also been experimentally used in animals in considerable quantities without any toxic symptoms occurring, we are obliged to look for some other cause of this acid intoxication.

Naunyn considers the condition of acetonæmia as not due to the presence of acetone in the blood, but that it is an acid intoxication resulting from various fatty acids in combination with diacetic and β-oxybutyric acids.

Brackett, Stone, and Law found in all their fatal cases the presence of fatty liver, and considered that this condition may have some influence in the production of the intoxication. Their autopsy findings were similar to those of Guthrie, and in one case of the series here reported the autopsy showed the presence of fatty liver. They, however, considered that fatty liver was not a sufficient cause for death, but that it, in connection with the acetonuria, was but the result of an acid intoxication, which also caused an excessive process of oxidation in the blood with resulting lack of oxygen, and that the three conditions combined may have had something to do with the fatal results. This apparent lack of oxygen is borne out by the statement of Brewer, in describing the "air hunger" found in this condition, which "was evidenced by increased rapidity and depth of respirations, with a bright red color of the mucous membranes and the skin, due to the presence of aërated blood in the veins from inability to absorb carbon dioxide from the tissues."

In a study of these cases, it is apparent that, following some profound change suddenly taking place, the cause of which is not yet determined, there occurs a rapid change in the body metabolism, which is shown by the presence in the urine and blood of acetone, diacetic and β-oxybutyric acids in varying quantities, associated with clinical signs and autopsy findings which have been similar to a more or less degree in all cases. What the cause is operating to produce this change in the body metabolism has not yet been determined; whether it is due to an increased destruction of proteid matter, as Heurter claims, it nevertheless remains that the condition termed aciduria, acetonuria, acetonæmia, is doubtless one of a severe acid intoxication. Edsall claimed that no specific toxic agent is at work, but that the condition is due to an excessive amount of acids due to the reduction of the alkalinity of the tissues and body fluids, and that this was produced by the acids carrying off the alkalies in combination with them, and proposed as a rational treatment the administration of large quantities of alkalies to neutralize the excess of acids present. In the severe cases of the present series large quantities of bicarbonate of soda were given by mouth, intravenously and by rectum, without any amelioration of the clinical symptoms or any production of alkalinity of the urine.

None of the theories offered so far have been thoroughly satisfactory in explaining the cause of this condition of acid intoxication. While I do not attempt to explain the cause of the symptoms present, I would like to call attention to theories, that have been advanced of late, as to the causation of uræmia and eclampsia; and it may be, as our knowledge advances, there may be a similar etiological factor in the class of cases reported and uræmia and eclampsia. Landois, in speaking of the cause of these later conditions, considers that they may be produced by the action of a toxin or toxins on what he calls the psychomotor centres of the brain, and that at times there is a mechanical pressure on the same cortical centres. He has shown that toxins and other substances may produce all the symptoms of uræmia by local cortical action. Weisenberg found in two cases of uræmia, hemiplegia, extensive chromatolysis of the Betz cells of the paracentral lobe, and that cells in the anterior horns of the cord, medulla, cerebellum, and fibres of one motor tract showed pathological changes. Willson considers that the toxin theory cited above may play some part in the etiology of uræmia and eclampsia, and that there is another important influence at work in the form of intracranial and probably localized pressure on the psychomotor centres, and in support of this theory reports three cases. Tyson, in the discussion of Willson's paper at the meeting of the American Medical Association, June 9, 1904, thought that some toxic agent might be considered as responsible for the condition. Lambert, at the same meeting, considered that the lesions found in eclampsia to be identical with those of acute yellow atrophy of the liver. He also said that he has always noticed the apparent identity of the condition found in acute yellow atrophy of the liver and uræmia, that there was in uræmia signs of intracranial tension, and that apparently the same toxæmia was present in both conditions.

It may be that the condition of acid intoxication, whatever its cause, may be due to one similar to that found in uræmia and acute yellow atrophy of the liver. While the autopsy reports of the fatal cases at the Boston Children's Hospital do not show any evidence of intracranial pressure, yet the clinical symptoms in some of the cases were certainly those of cerebral pressure, and all were associated with fatty liver. In Guthrie's series the autopsy reports of the fatal cases showed the condition of fatty liver and clinical signs of cerebral pressure. Several cases of this series observed at the Boston City Hospital were undoubtedly due to some cerebral lesion, and were treated as cerebral concussion. Whether the theory of intracranial pressure has any bearing in the production of the symptoms of acid intoxication will only be determined by a study of future cases and experimental research.

Tests used for Acetone and Diacetic Acid.—The test used for determining the pressure of acetone in the urine is as follows: To five cubic centimetres of urine are added a crystal of sodium nitroprussiate and sufficient sodium hydrate to render the solution strongly alkaline. This is thoroughly shaken up in a test-tube. On the addition of glacial acetic acid, the presence of acetone is shown by the occurrence of a purple color to the foam.

The presence of diacetic acid is shown by a Burgundy red color appearing on the addition of a strongly aqueous solution of ferric chloride to the urine.

No quantitative examination of the urine was made in any of the cases of the series, but the amount was roughly determined by the depth of color occurring in making the qualitative tests.

Statistics.—Of the 400 cases observed at the Boston City Hospital, symptoms of acid intoxication were present in forty-six. Of the forty-six cases, acetone and diacetic acid, separately or combined, were found in the following conditions: 11 cases of appendicitis; 14 of contusions and fractures; 2 of gastric disease; 2 of carcinoma; 3 of severe lacerated contused wounds; 2 of localized septic processes; 2 of cerebral concussion; 1 of salpingitis; 1 of acute multiple suppurative osteomyelitis; 1 of floating kidney; 1 of fæcal fistula and enterocolitis; 1 of epilepsy; 1 of tuberculous cervical noditis; 1 of burns and typhoid fever; 1 of diabetic gangrene; 1 of hæmorrhoids, and 1 of alcoholism.

In seventeen cases symptoms were present on entrance; in twelve cases, within twenty-four to forty-eight hours after the administration of a general anæsthetic, ether being used in ten cases and nitrous oxide in two cases; in seventeen cases symptoms were not present at time of entrance, but developed later without any anæsthetic being administered, and for which no cause could be assigned. Acetone and diacetic acid were present in the urine at the same time in twenty-four instances; acetone alone was present in twenty cases; diacetic acid alone occurred in two cases; acetone, diacetic acid, and sugar were present together in three cases; and acetone and sugar were together present in one case. In these forty-six cases there were six deaths.

Symptoms.—In those cases in which the condition developed a number of days after entrance and the onset could be carefully noted, the first symptom to attract attention was a peculiar apathy. This was accompanied by a marked sweetish odor to the breath, a distaste for food, slight increase in the body temperature, and in most cases vomiting.

The odor to the breath was of a peculiar, pungent, fleeting odor, or that of acetone, which at times suggested chloroform. In some cases it was very faint and could only be detected very close to the patient's mouth, in others it would be so strong as to be noticeable quite a distance from the patient's bedside. The odor became so characteristic of the condition, that after a time, when apparently there was no other symptom present, and nothing else to indicate the condition of acetonuria, on going to the bedside and catching the faint peculiar odor, it could be definitely stated that an examination of the urine would show the presence of acetone and diacetic acid.

The vomiting would occur without apparent cause, would follow immediately on taking anything into the stomach; in the mild cases it was colorless, copious, and watery in character, having a foul acid odor, contained particles of semidigested food, and in the severe cases was dark, bile-stained, of a "coffee-ground" appearance, and continued so until death. The pulse was increased in rapidity, of decreased tension, and in some cases became very weak. An absence of fever was noticeable excepting in severe cases, when the temperature would reach 102° to 103°. Alternating with the apathy there would be periods of restlessness, during which the patient required constant attention lest he fall out of bed or tear off his dressings. The face would be alternately pale or flushed, and at times expressive of considerable anxiety. In the fatal cases consciousness usually remained until near the end. From periods of restlessness, the patient would sink into a condition of stupor, or become delirious; the vomiting would cease, cyanosis generally occurring just before death, and the respiration and the pulse gradually failed, the latter often becoming imperceptible just before breathing ceased. Several cases complained of photophobia and dimness of vision, notably Case XL.

The urine in the fatal cases was always diminished in amount, at times turbid, of high specific gravity, and in several cases contained a trace of albumen.

In the mild cases the patients complained of being drowsy and weak. There was a marked odor of acetone to the breath in all cases. The vomiting varied in amount and was not present in all cases. The tongue was dry, clean, and red. The urine always contained acetone and diacetic acid separately or together. These symptoms would last from two to three days, and usually without any special treatment, excepting the exclusion of mouth feeding, would disappear.

A number of cases in which symptoms were present on entrance were those that had sustained an injury. These cases were usually dull, apathetic, had the peculiar odor to the breath, occasionally slight vomiting, and the presence in the urine of acetone and diacetic acid. This condition would last twenty-four to forty-eight hours, and suddenly all symptoms would disappear, and the examination of the urine would show the absence of acetone and diacetic acid. Just what bearing the injury had upon the etiology of the condition it is impossible to say, excepting that there may have been some cerebral congestion present to account for the symptoms.

The case operated on for floating kidney was noteworthy for the fact that the condition did not appear until after operation, and it may be that the resulting active congestion of the kidney had some influence in the formation of toxins, which should have been eliminated by that organ, and which caused the resulting train of symptoms.

A number of cases developed symptoms after they had been in the wards many days. In these the condition could not be ascribed to injury, anæsthesia, or diet. Their mode of life in the wards was similar to that of other patients, and some of the cases had entirely convalesced and were awaiting their discharge. While most of these cases occurred in children, no cause can be assigned for its development.

Treatment.—In the mild cases, in many instances, there was no special form of treatment adopted. If vomiting occurred, mouth feeding was prohibited; and if the condition lasted several days, nutrient enemata were given every four to six hours. Other mild cases were given bicarbonate of soda in large doses, but apparently without any marked relief in the symptoms, as compared with those not treated in this way. In the severe cases bicarbonate of soda was given by mouth; if retained, by enemata, subcutaneously and intravenously, and while for a short time there was some hope of this form of treatment doing good, it was usually of but temporary relief. In fact, in the severe cases the urine nearly always remained acid in spite of treatment. In addition the severe cases were treated symptomatically. The best results were obtained by the use of adrenalin chloride, as shown in Case I. This was given subcutaneously every eight to twelve hours; in children about 200 cubic centimetres of a 1-50,000 adrenalin saline solution, in adults 500 cubic centimetres, were used. The effect of this was shown by a marked increase in tension and slowing of the pulse; the cyanosis present would be replaced by a rather excessive ruddy appearance; the apathy would become less, and the general condition markedly improved. The effect of this stimulation would last three to four hours; and, while it was not given simply on account of the acid intoxication, it was followed by such good results as shown by the improved general condition that in all severe cases it was eventually used. To relieve the thirst, enemata of salt solution were given every six hours, alternating with nutrient enemata.

From a study of the cases, it is impossible to say that any special treatment had any direct effect upon the condition present, and the results obtained depended upon stimulation and symptomatic treatment.

The cases in detail are as follows:

CASE I.—*Acute Appendicitis.*—O. M.; aged nine years; school-boy. Admitted May 16, 1904. Service of Dr. H. W. Cushing. Family History. Negative. Previous History. Pneumonia three years ago, followed by measles and bronchitis. Severe cough the past four to five months.

Present Illness.—General malaise beginning three days ago. Vomiting began two days ago and has continued. Complained of feeling feverish yesterday. General abdominal pain began yesterday, localized in right iliac fossa this morning. Patient unable to retain anything by mouth during the past two days. Mother has noticed peculiar odor to breath the past two days.

Physical Examination.—Well developed and nourished. Face anxious and pale. Extremities cold. Pupils react equally to light. Tongue dry, red, thin yellowish coat. Mucous membrane pale. Sweetish odor to breath. No general glandular enlargement. Pulse equal, regular, of fair volume and tension, 160. Heart and lungs negative. Abdomen markedly retracted. Considerable tenderness over McBurney's point. Moderate spasm over entire right side of abdomen. General condition critical. Leucocytes, 31,400. Strychnine sulphate, $^1/_{40}$ subcutaneously, given on entrance on account of patient's condition.

Operation.—May 16, 1904, one hour after entrance. Ether. Dr. Cushing, Dr. Kelly. Vertical incision about two and one-half inches at outer border of rectus muscle, upper angle at level of umbilicus. On opening peritoneum, intestines found to be collapsed and of a grayish red color, suggesting condition found in a cadaver. Appendix retrocæcal and running upward, entirely free, slightly enlarged, and serous coat slightly injected; slight increase in circumference at middle. Appendix removed and stump touched with carbolic acid (95 per cent.) and alcohol. As condition of appendix did not seem to account for patient's serious condition, entire abdomen was explored, but nothing abnormal found. Abdominal cavity filled with normal salt solution. Sterile gauze wick to pelvis and a second one to stump of appendix. Incision closed with through-and-through interrupted silkworm gut except at point of drainage.

On opening appendix there was found, about two centimetres from tip, an area about one centimetre in diameter, of slight œdema and redness of mucosa, lumen of appendix containing a grape seed.

Patient's general condition was so grave after operation that he was given subcutaneously 250 cubic centimetres (1-50,000) adrenalin salt solution, which was followed shortly by marked improvement in pulse and general condition. Very restless after operation. Urine obtained before operation showed, color, pale; specific gravity, 1018; reaction, acid; no albumen; no sugar. Acetone present, diacetic acid absent.

May 18. Since operation sweetish odor of breath continues. Patient mildly delirious and at times very drowsy. Adrenalin salt solution, 250 cubic centimetres (1-50,000), given subcutaneously every twelve hours. Urine contains acetone and diacetic acid. Vomiting continues. Abdomen not distended. Placed on nutrients. Peptonized milk, six ounces; brandy, two ounces; salt solution, two ounces; egg, one; Tr. opii deod., gtt. iii.

May 19. Leucocytes, 11,400.

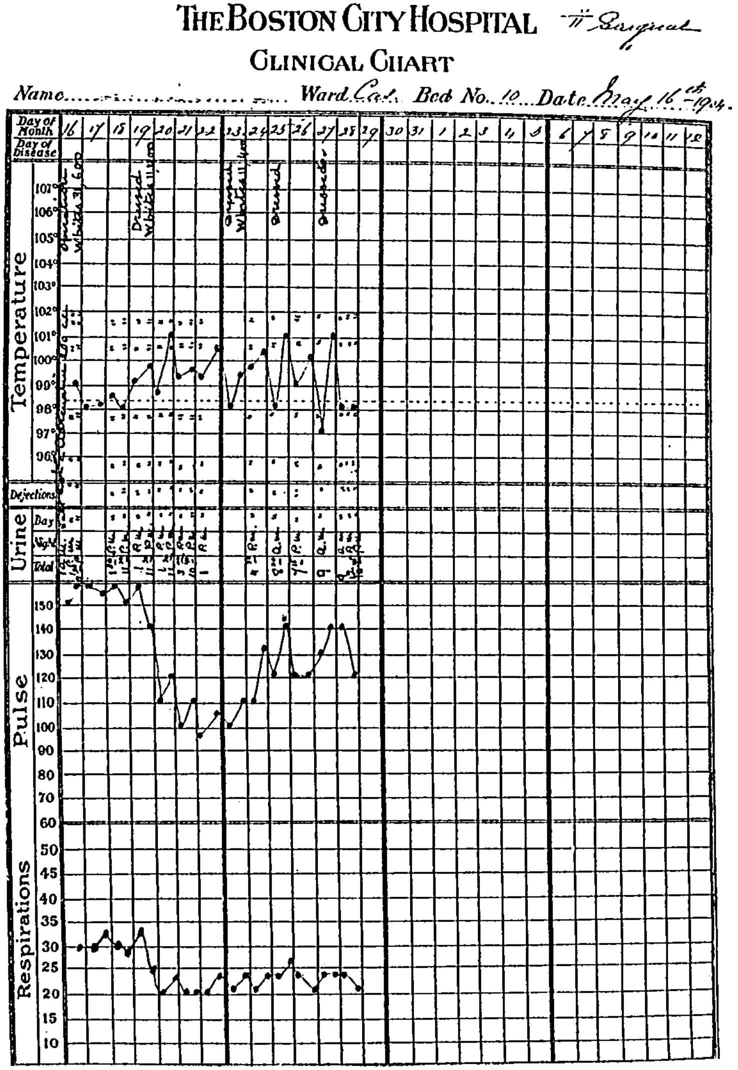
May 22. General condition markedly improved. Pulse-rate has gradually fallen to 120. Adrenalin salt solution continued every twelve hours subcutaneously. Still occasional vomiting. Acetone and diacetic acid present in urine. Odor of acetone still on breath. Delirium absent, although patient is still drowsy and resists dressing daily. Wicks started on third day and gradually shortened daily.

May 23. Leucocytes, 12,400.

May 26. Soda bicarbonate, gr. xxx, every two hours by mouth. Nutrients and adrenalin continued. Still occasional vomiting. Patient much brighter since last note. Pulse-rate steadily rising. Vomiting continues. Slight delirium yesterday. To-day expression is dull; patient sleeping most of the time; refuses everything by mouth. Odor present on breath. Acetone and diacetic acid still present in urine. Soda bicarbonate, two ounces, given intravenously yesterday and to-day. Adrenalin and nutrients continued. Dressing changed daily. Two wicks. No abdominal distention. Patient slowly failed and, in spite of active stimulants, died at 11.05 P.M.

No autopsy. Examination of liver at time of operation apparently normal.

The effect of the continued use of adrenalin salt solution is shown in the appended temperature chart. It was given every twelve hours from time of entrance. The pulse-rate remained



THE BOSTON CITY HOSPITAL — II Surgical

CLINICAL CHART

Name.................... Ward Cal. Bed No. 10 Date May 16th 1904.

at 160 for four days, then gradually decreased, and at time of death was only 120.

Throughout the entire course of the disease the patient remained conscious, although periods of apathy alternated with those of extreme restlessness, during which he would utter the most piercing shrieks, required most careful watching, and at times of changing his dressings it was impossible to do so with any degree of asepsis. The odor of acetone could be noticed throughout the room at all times. The urine the last four days was very much diminished and of high color.

CASE II.—*Contused Lacerated Wound of Foot.* (*Measles.*) —A. S.; aged four years. Admitted May 27, 1904. Service of Dr. H. W. Cushing.

Present Illness.—While mother was getting on car, the latter started, and child's foot caught under wheel.

Physical Examination.—Negative save for local condition. On dorsum of foot is a contused lacerated wound extending down to tendon sheaths, an irregular lacerated wound on plantar surface extending from toe to heel. Considerable laceration of plantar muscles. Compound dislocation of first phalangeal joint of great toe. Fracture of proximal phalanx of fifth toe.

Operation.—May 27, 1904. Ether. Dr. Kelly. Repair under aseptic conditions. Great toe amputated at terminal joint, fifth toe at metatarsophalangeal joint. Sterile dressing. Plaster-of-Paris bandage.

Examination of urine day after operation. Color, pale; specific gravity, 1025; albumen and sugar absent. Acetone and diacetic acid present. Odor of acetone to breath. No other symptoms.

May 31. Acetone present (slight). Diacetic acid absent.

June 3. Acetone and diacetic acid absent.

June 10. Patient developed measles, and was transferred to South Department. No special treatment.

CASE III.—*Fracture of Femur; Refracture.* (*Measles.*)— L. N.; aged four years. Admitted April 21, 1904. Service of Dr. H. W. Cushing. Previous History. Fracture of femur, August 11, 1903. Discharged in October, 1903. Using leg past two months without crutches.

Present Illness.—Patient fell to-day, April 21, 1904, and refractured femur. Given ether for reduction and immobilization. Urine examined April 21 and May 20, 1904, acetone and diacetic acid present.

June 15. Loss of appetite. Patient drowsy. No delirium. Odor of acetone to breath. Urine examined and found to be as follows: Pale; 1027; acid; albumen and sugar absent. Acetone and diacetic acid present. No special treatment.

June 18. Measles developed. Patient apathetic, vomited several times. Marked odor of acetone to breath. Drowsy, no delirium, urine scanty, high colored. Acetone and diacetic acid present.

June 20. Discharged to parents, as latter refused to allow child to go to South Department.

CASE IV.—*Appendicitis; Diffuse Peritonitis.*—M. F.; aged eleven years; school-girl. Admitted May 11, 1904. Service of Dr. H. W. Cushing. Family History. Negative. Previous History. Negative.

Present Illness.—First symptoms evening of May 10. Pain in epigastrium leaving this region and centring at McBurney's point. Nausea, vomiting. Temperature, 99.5° F.; pulse, 100.

Physical Examination.—Abdomen slightly distended, spasm entire right side, tenderness on pressure, greatest at McBurney's point. Leucocytes, 19,200.

Operation.—May 11, 1904. Ether. Dr. Cushing, Dr. Kelly. Fifteen hours after onset of symptoms. Vertical incision outer border of rectus muscle. Appendix up and outward behind cæcum, united to cæcum by newly formed adhesions, serosa covered with fibrin, appendix generally enlarged, no perforation. Free cloudy fluid in pelvis and extending upward on right side about appendix. Appendix removed, abdominal cavity irrigated with normal salt solution, and drained with sterile gauze wicks. Culture from fluid in pelvis showed streptococci and Bacillus coli communis. Good recovery from ether. Good convalescence. Urine negative until June 22, when acetone and diacetic acid were found. Two days previous patient gradually became drowsy, and, although she had been up and about the ward for from seven to ten days, went to bed. Marked odor of acetone to breath, vomiting, inclined to sleep. Placed on liquid diet. Patient given soda bicarbonate, gr.

xxx, every two hours until she was unable to retain anything in stomach.

June 28. General condition has improved, vomiting stopped, although patient was still apathetic and had slight odor of acetone to breath.

July 1. Still slight odor to breath, no other symptoms. Patient discharged to father on request.

CASE V.—*Fracture of Femur.*—C. E. S.; aged twenty-three years; hostler. Admitted March 26, 1904. Service of Dr. H. W. Cushing. Family History. Negative. Previous History. Negative.

Present Illness.—Yesterday, while at work, a bale of hay fell three stories to the sidewalk and bounced, striking patient under the chin; patient was thrown out into the street, sustaining fracture of right femur, and was rendered unconscious. Ether given March 27, and Buck's extension apparatus applied.

March 28. Urine, color normal; 1025; acid; no albumen; no sugar.

April 7. Urine, color normal; 1030; no albumen; sugar, one per cent. No acetone. No diacetic acid present. Patient drowsy. Loss of appetite, thirst, nausea; no vomiting. No odor to breath.

April 9. Urine again examined on account of clinical symptoms. Color, normal; 1030. Slight possible trace of albumen; sugar, one per cent. Acetone and diacetic acid present; present until April 14, when acetone and diacetic acid were absent from urine, and symptoms disappeared. Soda bicarbonate given.

May 14. Discharged relieved.

CASE VI.—*Fracture of Femur.*—W. E. D.; aged eight years; school-boy. Admitted March 17, 1904. Service of Dr. H. W. Cushing. Family History. Negative. Previous History. Negative.

Present Illness.—Patient fell off fence eight feet to ground, fracturing right femur. Ether given March 17 and Buck's extension applied.

May 17. Up and about ward.

May 20. Patient began vomiting, became drowsy, odor to breath, thirst.

May 22. Urine, pale, cloudy; 1021; acid. Albumen very slight trace. Sugar absent. Acetone present. Diacetic acid absent; urine remained about the same until May 30, when acetone disappeared. Soda bicarbonate given until urine became alkaline.

May 30. Discharged to parents relieved.

CASE VII.—*Colles's Fracture.*—M. I. F.; aged fifty-seven years; single; housework. Admitted June 2, 1904. Service of Dr. G. H. Monks. Family History. Negative. Previous History. Negative.

Present Illness.—Patient tripped and fell on hand, receiving a Colles's fracture. Given nitrous oxide for reduction of fracture. Urine, June 2, after anæsthetic, color normal; 1022; acid; no albumen; no sugar. Acetone absent, diacetic acid present. No clinical signs.

June 3, 1904. Discharged relieved.

CASE VIII.—*Abscess of Leg.*—M. S.; aged thirty-one years; single; pickle-packer. Admitted June 2, 1904. Service of Dr. F. S. Watson. Family History. Negative. Previous History. Negative.

Present Illness.—Leg ulcer for past five years, which has at times been healed. Abscess of leg, inner side, above internal malleolus.

June 2. Urine, high color; 1020; acid; no albumen; no sugar. Acetone absent, diacetic acid present.

Operation.—June 4, 1904. Ether. Dr. Hollister. Abscess incised. No clinical symptoms after operation, excepting slight odor to breath, which continued for two days. No special treatment.

June 5. Urine, color normal; 1019; acid; no albumen; no sugar. Acetone and diacetic absent.

July 29. Discharged relieved.

CASE IX.—*Gastric Ulcer.* (*Gastro-enterostomy, Posterior.*) —A. D.; aged thirty-one years; married; female; housework. Admitted June 11, 1904. Service of Dr. J. B. Blake. Family History. Negative.

Previous History.—Abdominal distress after meals, eructation of gas, and constipation for several years. Catamenia irregular (four to six weeks), very painful, and accompanied by vomiting. One year ago similar attack to present illness.

Present Illness.—For past five weeks patient has vomited almost immediately on ingestion of food. Considerable abdominal pain not localized. Vomitus consisted of non-digested food.

Physical Examination.—Slight epigastric tenderness. Pulsation of aorta easily felt. No evidence of aneurism.

Treatment.—Nothing by mouth but cracked ice. Nutrients every six hours. Suds enema daily.

June 12. Urine negative.

June 15. Nauseated at times since entrance. Yesterday, four minims 4 per cent. solution cocaine, and five grains cerium oxalate every four hours for control of nausea. No vomiting to-day; slight nausea during night.

June 19. Vomited at times, vomitus being streaked with blood; cocaine and cerium oxalate omitted on account of irritation. Bismuth tried and omitted.

June 23. Light diet without discomfort. No nausea.

June 27. Operation. Ether. Dr. Blake. Gastro-enterostomy, posterior

June 28. Pulse, 120, poor quality. Patient vomited two ounces of bright blood. Patient given beef-juice in two-ounce doses. As this caused nausea, it was omitted. Again vomited blood. Morphine and adrenalin solution subcutaneously.

June 29. Abdomen distended. Pulse, 140; temperature, 100° F. Wound dressed, clean. Distention less at 6 P.M. Adrenalin solution again given, followed by improvement in pulse, then 120. Urine to-day showed presence of acetone. Diacetic acid absent. Pale, 1013. Trace of albumen.

June 30. Patient died, vomiting continuing until death. No trace of acetone in urine obtained post-mortem.

No autopsy performed.

CASE X.—*General Contusions.*—E. T. P.; aged sixty-five years; widower; no occupation. Admitted June 25, 1904. Service of Dr. F. S. Watson. Family History. Negative. Previous History. Treated five years ago for diabetes. Convulsions at irregular intervals since.

Present Illness.—Patient fell yesterday on stairway (Sullivan Square subway), striking head on railing. Unconscious until ambulance arrived, about twenty minutes.

Physical Examination, Local.—Small lacerated wound of face and forehead, aseptic dressing. No anæsthetic given. Urine, pale; 1031; acid; no albumen; sugar, 2 per cent. Acetone and diacetic acid present. Slight odor to breath; no other symptoms. Examination of urine remained unchanged the day of discharge. No special treatment.

June 29. Discharged relieved.

Case XI.—*Floating Kidney.*—E. F.; aged twenty-nine years; married; housework. Admitted June 9, 1904. Service of Dr. J. B. Blake. Family History. Negative. Previous History. Symptoms of floating kidney for past fourteen years.

Physical Examination, Local.—Easily palpable right kidney.

June 9. Urine negative.

June 10. Operation. Nephrorrhaphy. Ether. Dr. Blake.

Urine.	Color.	Specific Gravity.	Re-action.	Albumen.	Sugar.	Acetone.	Diacetic Acid.
June 11	Normal.	1019	Acid.	Slight trace.	0	Faintly.	Absent.
" 12	Normal.	1018	Acid.	Trace.	0	Very marked.	Present.
" 13	Normal.	1020	Acid.	Slight trace.	0	Markedly present.	Present.
" 14	Normal.	1019	Acid.	Slight trace.	0	Present.	Absent.
" 15	Normal.	1019	Acid.	Slight trace.	0	Faintly present.	Present.
" 16	Normal.	1019	Acid.	Sl. pos. trace.	0	Absent.	Absent.
" 19	Normal.	1019	Acid.	Sl. pos. trace.	0	Very faintly pres.	Absent.

To determine the effect of trauma to the kidney in this operation in reference to the production of acetone and diacetic acid in the urine, an examination was made daily. The report of each examination is noted above. While acetone and diacetic acid were present in variable quantities, at no time were there any clinical signs of an acid intoxication. The patient had an uninterrupted convalescence.

Case XII.—*Appendicitis, Acute, with Abscess.*—J. G.; aged sixty-five years; male; married; night watchman. Admitted May 29, 1904. Service of Dr. J. B. Blake. Family History. Negative. Previous History. Negative.

Present Illness.—Four days ago pain in right lower quadrant of abdomen. Vomiting daily since. Diarrhœa from onset.

Physical Examination.—Spasm on right side of abdomen. Indefinite mass, size of an orange, felt in region of appendix. Leucocytes, 16,400.

May 30. Urine, normal; 1024; acid; no albumen; sugar, 1.6 per cent. Acetone present, diacetic acid absent.

June 1, 1904. On account of presence of acetone in urine, general anæsthesia was not considered advisable. Schleich's fluid used 1–1000. Appendix, abscess found. Appendix not removed. Abscess cavity drained. No symptoms of acetonuria.

June 12. Sugar, 1.38 per cent. Acetone slight. No diacetic acid.

June 20. Sugar, 1.2 per cent. Acetone absent. Diacetic acid absent. Patient convalescing.

Case XIII.—*Cerebral Concussion.*—H. F.; aged seven years; school-boy. Admitted June 6, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient run into by another boy two days ago, being thrown to ground, striking head. Not unconscious. Brought into hospital to-day on account of drowsiness, incoherence, and slight abdominal pain.

Physical Examination.—Slight laceration over occiput. A second one over right frontal region. Abrasion of right side of nose. Slight abdominal tenderness which is general. Odor of acetone to breath. Principal symptoms are mental, chiefly drowsiness and inability to think clearly. Mistakes are made in counting and in naming objects seen. Vomited several times while in hospital.

June 6. Urine slightly pale; 1018; acid; no albumen; no sugar. Slight amount of acetone present. No diacetic acid. Urine examined was the first passed.

June 8. No cerebral symptoms. Odor of acetone gone. Urine negative. Discharged relieved.

Case XIV.—*Appendicitis, Acute, with Abscess.*—S. B.; aged fifty years; widow; housework. Admitted June 7, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Abscess of kidney twenty-four years ago (?), told so by physician. Stone removed from bladder fifteen years ago.

Present Illness.—Pain and tenderness over right side of abdomen and vomiting past two days.

Present Examination, Local—Some spasm and tenderness of right lumbar region extending into back and up towards region of gall-bladder. Dulness and resistance in right lumbar region near region of right kidney and extending to region of appendix. Point of greatest tenderness in lumbar region, outer border of erector spinæ muscles. Leucocytes, 18,000. Odor of acetone to breath. Patient drowsy.

June 8. Urine slightly high and cloudy; 1020; alkaline; no albumen; no sugar. Acetone and diacetic acid present.

June 15. Urine negative.

June 17, 1904. Operation. Ether. Dr. H. A. Lothrop, Dr. Kelly. Incision outer border of erector spinæ muscles. Abscess cavity containing about two ounces of pus; at bottom of abscess appendix could be felt, and was apparently retroperieoneal. Appendix not removed. Abscess cavity drained. Uninterrupted convalescence.

July 10. Discharged relieved.

Case XV.—*Cerebral Concussion.*—J. M.; aged ten years; school-boy. Admitted June 15, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient fell off furniture wagon to ground, striking head and abdomen. No subjective symptoms of concussion excepting confusion of ideas for first twelve hours. Odor of acetone to breath on entrance.

June 17. Urine, normal; 1016; acid; no albumen; no sugar. Acetone present; diacetic acid absent.

June 19. Urine negative. No clinical symptoms.

June 20. Discharged relieved.

Case XVI.—*Fracture of Humerus; Fracture of Clavicle.*—K. B.; aged eight years; school-girl. Admitted June 18, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient fell two stories from a fire-escape, sustaining epiphyseal separation of upper end of right humerus and green-stick fracture of right clavicle. No clinical symptoms of acetone excepting a slight suggestion of odor to breath. Urine, normal in color; 1028; acid; no albumen; no sugar. Acetone and diacetic acid present. No anæsthesia given to apply fixation dressing.

June 20. Urine, color normal; 1026; acid; no albumen; no sugar. Acetone and diacetic acid absent. No clinical symptoms. No special treatment.

June 21. Discharged relieved.

Case XVII.—*Carcinoma of Uterus.*—E. P.; aged fifty-five years; married; housework. Admitted June 11, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Negative.

Present Illness.—Symptoms of uterine fibroid for past five or six years.

June 12. Urine, normal; 1023; acid; very slight trace of albumen; no sugar. Acetone and diacetic acid absent.

June 15. Operation. Ether. Dr. Bolles, Dr. Kelly. Hysterectomy. Pathological report shows carcinoma of the uterus near fundus, also several fibroids.

June 17. Urine, normal; 1020; acid; no albumen; no sugar. Acetone present, diacetic acid absent. Acetone odor to breath. Slight vomiting for four days after operation, then no signs of acetonuria clinically or in urine. Uninterrupted convalescence.

July 7, 1904. Discharged relieved.

CASE XVIII.—*Blank-Cartridge Wound of Hand.*—F. Q.; aged nine years; school-boy. Admitted June 17, 1904. Service of Dr. W. P. Bolles.

Present Illness.—While loading pistol with blank cartridge, the latter accidentally exploded, wounding the hand of the patient.

June 17, 1904. Operation. Ether. Dr. Kelly. Wound thoroughly curetted; antiseptic precautions. Urine passed that night showed color normal; 1022; acid. Albumen and sugar absent. Acetone and diacetic acid present. No clinical symptoms except slight odor to breath.

June 20. Urine. No acetone or diacetic acid present. Culture taken at operation showed absence of tetanus bacillus.

June 21. Discharged relieved.

CASE XIX.—*Lacerated Wounds of Hand from Cannon Cracker.*—M. O'B.; aged nine years; school-girl. Admitted June 18, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient picked up a lighted cannon cracker, the latter exploding in hand. Local examination; compound dislocation of thumb, palm of hand torn, exposing second metacarpal, first finger severely lacerated.

June 18. Operation. Ether. Dr. Kelly. Index-finger amputated at first joint, middle finger at terminal joint. Examination of urine passed night of operation was as follows: Color, normal; 1024; acid; no albumen; no sugar. Acetone and diacetic acid present. Acetone and diacetic acid persisted in urine three days. No clinical symptoms.

June 29. Discharged relieved.

CASE XX.—*Fracture of Ulna.*—B. D.; aged ten years; school-boy. Admitted June 30, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient, morning of entrance, fell from a fence, a distance of eight feet, falling on left forearm, sustaining a fracture of ulna and lacerated wound of forearm.

June 30. Operation. Ether. Dr. Kelly. Aseptic repair of wound; fracture found not to be compound. Examination of urine passed eight to ten hours after operation showed color pale; 1018; acid; no albumen; no sugar. Acetone and diacetic acid present. No clinical signs. Acetone and diacetic acid present in urine for two days.

July 6. Discharged relieved.

Case XXI.—*Fracture of Tibia.*—K. C.; aged twenty-seven; female; single; housework. Admitted July 1, 1904. Service of Dr. Paul Thorndike.

Present Illness.—Two days before admission patient fell down steps and turned on foot, sustaining fracture of middle of right tibia.

July 2. Urine, light color; 1018; acid; no albumen; no sugar. Acetone and diacetic acid present. No anæsthetic given. No clinical signs. Acetone and diacetic acid present in urine for three days.

July 29. Discharged relieved.

Case XXII.—*Acute Multiple Suppurative Osteomyelitis.*—G. S.; aged twelve years; school-girl. Admitted April 4, 1904. Service of Dr. H. W. Cushing. Family History. Negative. Previous History. Negative.

Present Illness.—Patient unable to walk for past week on account of pain in right knee. Four days ago right thigh (lower third) and knee increased in size, accompanied by night cries, increased local temperature, pain, redness, and tenderness.

Physical Examination.—Well developed and nourished. Apprehensive. Face flushed. Tongue, white coat and dry. Pulse, 130; temperature, 102° F.

Local.—Right lower half of right thigh swollen, red, deep fluctuation, slight synovitis of knee.

Operation.—April 6, 1904. Ether. Dr. Hubbard, Dr. Kelly. Two lateral incisions over lower thigh, large quantity of pus evacuated. Periosteum stripped from bone. Culture showed pure culture of Staphylococcus pyogenes aureus. Urine, negative.

April 10. Second operation. Ether. Dr. Hubbard, Dr. Kelly. Left upper humerus, incision made and pus outside shaft, four trephine holes made, and pus found in medullary cavity (culture, Staphylococcus pyogenes aureus). Right lower femur trephined, pus found in medullary cavity (culture, Staphylococcus pyogenes aureus). Left lower femur trephined, no pus found (culture, Staphylococcus pyogenes aureus).

April 13. Third operation. Ether. Dr. Hubbard, Dr. Kelly. Lower end of right fibula trephined, pus outside bone and in medullary cavity (culture, Streptococcus pyogenes aureus, Staphylococcus pyogenes aureus, Bacillus subtilis). Blood culture, April 24, 1904, Streptococcus pyogenes aureus.

April 25. Parotid abscess incised. Ethyl chloride. Dr. H. W. Cushing, Dr. Kelly.

Repeated examinations of urine were made, and until May 9 acetone and diacetic acid were absent. On May 8 there was noticed a peculiar odor to the breath, accompanied by drowsiness, vomiting, and increased pulse-rate. Examination of the urine revealed the presence of acetone, and on the following day diacetic acid. The patient was given soda bicarbonate, gr. xxx, every two hours until she failed to retain anything by mouth, when she was given enemata containing soda bicarbonate, two ounces every four hours, until death, which occurred May 20. During the four days preceding death the patient was given subcutaneously 200 cubic centimetres of adrenalin salt solution (1–50,000) with slight favorable results. Nutrient enemata and stimulation were freely given. During the last four days patient had periods of restlessness alternating with stupor. The tongue remained a reddish color, and at all times was extremely dry. On account of screaming and apparent pain, sedatives were required, and towards the end vomiting ceased; the patient passed into a state of coma, the urine became very scanty, and death occurred very suddenly. Autopsy permission was not granted by parents. Patient died May 20.

Daily examinations of urine were as follows:

Urine.	Color.	Specific Gravity.	Reaction.	Albumen.	Sugar	Acetone.	Diacetic Acid.	Indican.
May 8	Slig'tly high	1020	Acid.	o	o	Absent.	Absent.	Absent.
" 9	Pale.	1018	Acid.	o	o	Present.	Absent.	Present.
" 12	Pale.	1014	Acid.	o	o	Present.	Present.	Present.
" 13	Cloudy.	1015	Acid.	o	o	Increasing.	Present.	Present.
" 14	Pale.	1015	Acid.	o	o	Present.	Present.	Present.
" 15	Pale, cloudy.	1015	Alkaline.	o	o	Not so marked	Present.	Absent.
" 16	Pale.	1017	Acid.	o	o	Present.	Present.	Absent.
" 17	Pale.	1015	Acid.	o	o	Present.	Present.	Absent.
" 19	Cloudy.	1017	Acid.	o	o	Present.	Present.	Absent.

CASE XXIII.—*Appendicitis.*—M. S.; aged thirty years; male; married; bricklayer. Admitted June 3, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Negative.

Present Illness.—Well until three days ago. Pain in left lower quadrant of abdomen, then in right. Bowels constipated. Slight nausea this morning.

Local.—Some tenderness on deep pressure in right iliac fossa. Leucocytes, 10,200. Urine, June 6, normal; 1026; acid; no albumen; no sugar. Acetone and diacetic acid present. Patient refused operation. No clinical symptoms present except odor to breath.

June 6. No symptoms of appendicitis since yesterday. Examination of urine negative. As patient desires to go home, he is discharged.

CASE XXIV.—*Compound Fracture of Tibia.*—P. H.; aged forty-six years; male; peddler. Admitted June 8, 1904. Service of Dr. F. S. Watson.

Present Illness.—Wheel of ice wagon went over left leg, causing compound fracture of tibia.

June 8, 1904. Operation. Ether. Dr. Hollister. Aseptic repair. Sterile dressing plaster-of-Paris bandage: Urine passed that night showed normal; 1024; acid; no albumen; no sugar. Acetone present, diacetic acid absent. No clinical symptoms present excepting odor to breath.

July 8. No symptoms since operation. Acetone present in urine two days.

CASE XXV.—*Fracture of Fibula.*—J. G.; aged thirty-three years; male; hair-dresser. Admitted June 9, 1904. Service of Dr. F. S. Watson.

Present Illness.—Patient turned ankle stepping from street to curb. Urine, June 11, normal; 1022; acid; no albumen; no sugar. Acetone present, diacetic acid absent. No clinical signs. Presence of acetone discovered in routine examination.

June 12. Acetone and diacetic acid absent.

June 20. Discharged relieved.

CASE XXVI.—*Appendicitis, Acute, with Abscess.*—J. D.; aged twenty-five years; warehouseman. Admitted June 11, 1904. Service of Dr. F. S. Watson.

Present Illness.—Two days ago pain in abdomen. Vomited several times during first two days; none since. Bowels open. Pain decreasing until to-day, when it grew worse.

Local Examination.—Abdomen moderately distended. Tenderness and muscular spasm on right, a distinct tender mass in right lower quadrant, region of appendix. Leucocytes, 21,400.

Operation.—June 11, 1904. Ether. Dr. E. H. Nichols. Abdomen opened. Appendix found to be long, ruptured, and gangrenous, surrounded by an abscess cavity. Urine passed June 11 showed high; 1035; acid; no albumen; no sugar. Acetone present, diacetic acid absent. No clinical symptoms. No further examination of urine made. Uneventful convalescence.

Case XXVII.—*Diabetes; Gangrene of Foot.*—G. W.; aged sixty-six years; expressman. Admitted June 10, 1904. Service of Dr. F. S. Watson.

Local Examination.—Left hand shows small ulceration of third and fourth fingers. Right toe shows ulceration size of dime on inner side of metatarsophalangeal joint. Ulcer clean and surrounded by a reddened area. Left foot, the fourth and fifth toes, all cold and black, in a condition of dry gangrene. Urine, June 15, before operation, normal; 1023; acid; no albumen; sugar present, 1.70 per cent. No acetone, no diacetic acid.

Operation.—June 15, 1904. Ether. Dr. F. S. Watson. Amputation of left leg just above knee-joint. Urine passed June 20, normal; 1036; acid; no albumen; no bile; sugar, 1.80 per cent. Acetone and diacetic acid present. No clinical symptoms.

June 26. Examination of urine negative, excepting sugar present 1 per cent.

July 10, 1904. Discharged relieved.

Case XXVIII.—*Appendicitis, Acute Catarrhal.*—N. M.; aged twenty-one years; male; painter. Admitted June 20, 1904. Service of Dr. F. S. Watson. Previous History. First attack six months ago.

Present Illness.—Sudden pain in abdomen three days ago. Bowels constipated until yesterday, when moved by an enema. No vomiting. Pain is now confined to right lower quadrant of abdomen.

Local.—Tenderness on deep pressure in right lower quadrant of abdomen. No muscular spasm. Nothing felt.

June 21. Urine normal; 1022; acid; no albumen; no sugar. Acetone present, no diacetic acid. Slight odor of acetone to breath. Leucocytes, 8800.

Operation.—June 22, 1904. Ether. Dr. F. S. Watson. Appendix found to be in a condition of mild inflammation. Appendix removed.

June 25. Urine negative. Normal convalescence.

Case XXIX.—*Fracture of Femur.*—A. R.; aged fifty-two years; female; housework. Admitted June 20, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Fell from an electric car, fracturing left femur.

June 21. Urine, normal; 1010; acid; albumen, very slight trace. No casts. Normal and abnormal blood. No sugar. Acetone and diacetic acid present, found in routine examination.

June 23. Urine negative, except slight trace of albumen. No clinical symptoms. No anæsthetic given for application of extension apparatus.

Case XXX.—*Alveolar Abscess.*—F. G.; aged twenty-two years; travelling salesman. Admitted May 3, 1904. Service of Dr. A. Post.

Present Illness.—Tooth began to ache seven days ago. Extracted two days ago. Face began to swell six days ago.

Local Examination.—Entire right side of face shows swelling and brawny induration with but little tenderness. Patient unable to open mouth.

June 1. Urine, high colored; 1030; acid; no albumen; no sugar. No acetone, no diacetic acid.

Operation.—June 1, 1904. Nitrous oxide. Dr. Hollister. Incision.

June 2. Urine, high; 1030; acid; no albumen; no sugar. Acetone present, no diacetic acid found in routine examination.

June 3. Urine negative. No clinical symptoms.

Case XXXI.—*Appendicitis, Acute, with Abscess.*—H. P.; aged twenty-five years; female; book-keeper. Admitted June 17, 1904. Service of Dr. F. S. Watson.

Present Illness.—Three days ago at night sudden onset of cramp-like pains in lower abdomen. Diarrhœa and vomiting. Vomiting continued for three days, vomitus yellow liquid. Diarrhœa lasted twenty-four hours. One movement yesterday, following administration of castor oil. Vomited everything but soda water taken last night. Pain in centre of abdomen continued same as at onset.

Local.—Slight increased spasm on right. Tenderness across entire lower half of abdomen. Leucocytes, 19,000.

June 19. Urine (turbid), 1030; acid; slight trace of albumen; no sugar. Acetone present, no diacetic acid found in routine examination.

June 20. Same as day before, plus presence of diacetic acid. No clinical signs except odor to breath.

June 21. Tenderness was marked in right lower quadrant.

Operation.—June 29, 1904. Ether. Dr. E. H. Nichols. McBurney incision. Gangrenous appendix with abscess. Appendix removed; drainage.

June 29. Urine negative. Normal convalescence. Acetone present in urine seven days.

Case XXXII.—*Epilepsy.*—T. S.; aged thirteen years; male; no occupation. Admitted June 13, 1904. Service of Dr. F. S. Watson. Family History. Negative.

Previous History.—At thirteen months began to have convulsions; had them until three years old; then none until nine years old. Pneumonia nine years ago. Malaria five years ago.

Present Illness.—Since malaria five years ago has had convulsions. Attacks come on while standing up, when he will fall; bites tongue. During the past three weeks has talked incoherently, and laughs to himself; has been getting very weak and losing weight; has several convulsions a day. Attacks last from two to three minutes. Appetite capricious.

Physical Examination.—Well developed and poorly nourished. Stellate scar in left eyebrow. On right postparietal region a tumor three centimetres in diameter closely adherent to skull, over which the skin moves; indefinite sense of fluctuation in tumor. Epileptic attacks since entrance.

June 14. Urine, color normal; 1020; acid; no albumen; no sugar; no acetone; no acetic acid.

Operation.—June 15, 1904. Ether. Dr. E. H. Nichols. Tumor dissected out. Pathological report, chronic inflammatory.

June 18. Urine, normal; 1022; acid; no albumen; no sugar; acetone present; no diacetic acid.

June 20. Acetone absent.

June 27. No convulsive attacks since operation. Urine negative. Discharged relieved.

CASE XXXIII.—*Tuberculous Cervical Noditis.*—H. D.; aged sixteen years; female; housework. Admitted June 3, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Negative.

Present Illness.—Patient has noticed swellings of both sides of neck since age of nine years, swelling increasing in size every winter.

Local Examination.—Swelling size of small egg just below left ear and another just below this at base of neck. Below right ear there is a fluctuating swelling the size of a walnut.

June 4. Urine, slightly high and cloudy; 1019; acid; no albumen; no sugar; acetone present. No diacetic acid found in routine examination. No clinical symptoms.

Operation.—June 9, 1904. Ether. Dr. H. A. Lothrop, Dr. Kelly. Dissection of glands.

June 8–12. Urine negative. Pathological report, tubercular lymph-nodes.

June 21. Discharged relieved.

CASE XXXIV.—*Appendicitis, Chronic, with Adhesions; Inguinal Hernia.*—W. B.; aged twenty-six years; physician. Admitted June 10, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Inguinal hernia for past six years. During the past nine months has had eight attacks of appendicitis.

Present Illness.—Pain, colicky, past four days; tenderness over appendix region, also in lumbar region. No vomiting. No digestive disturbance.

June 10. Urine, normal; 1025; acid; no albumen; no sugar; acetone present. No diacetic acid found in routine examination. No clinical signs.

Operation.—June 18, 1904. Ether. Dr. H. A. Lothrop, Dr. Kelly. Appendectomy. Bassini operation on hernia. Pathological report of appendix, chronic obliterative appendicitis. Uneventful convalescence. Subsequent examinations of urine negative.

July 12. Discharged relieved.

CASE XXXV.—*Fracture of Radius.*—D. S.; aged seven years; school-boy. Admitted June 11, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Negative.

Present Illness.—Patient fell off roof, fifteen feet, to ground, sustaining slight abrasion of face and fracture of lower end of left radius.

June 11. Urine, normal; 1025; acid; no albumen; no sugar. Acetone present; diacetic acid present in small amount. No clinical signs except odor of breath.

June 13. Urine negative. Ether given two days after admission for reduction of fracture.

June 18. Discharged relieved.

CASE XXXVI.—*Fracture of Pelvis.*—S. P.; aged fourteen years; male; clerk. Admitted June 18, 1904, to Relief Station, Boston City Hospital. Transferred to Main Department, Boston City Hospital, June 20, 1904. Service of Dr. W. P. Bolles.

Present Illness.—Patient is said to have fallen off his team and been run over by another team.

Physical Examination.—Well developed and nourished. Pale; hysterical. In considerable shock. Pulse rapid and weak. Considerable general tenderness of abdomen. Voluntary spasm. Contusion and abrasion of right flank. Ecchymosis of left groin. Crepitus in left pelvis. Considerable swelling of left thigh. Rectal examination shows fracture of descending ramus of left pubis and of fragment in immediate neighborhood of anterior wall of rectum.

June 20. Urine passed, normal; 1023; acid; no albumen; no sugar. Acetone present; no diacetic acid. No clinical signs except odor to breath. June 23. Urine negative. July 10. Convalescing.

CASE XXXVII.—*Salpingitis.*—G. C.; aged twenty-one years; table-girl. Admitted June 25, 1904. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Colicky pains in lower abdomen at menstrual period.

Present Illness.—During past month has had occasional slight pain in right lower abdomen, which increased in severity past four days.

Local Examination.—Slight tenderness in right suprapubic region, slight vaginal discharge.

June 26. Urine passed, normal; 1020; acid; no albumen; no sugar. Acetone and diacetic acid present. No clinical signs but odor to breath.

June 29. Urine negative. Discharged relieved. No operation.

CASE XXXVIII.—*Carcinoma Descending Colon; Intestinal Obstruction.*—F. M.; aged twenty-nine years; married; housework. Admitted May 22, 1904. Service of Dr. Paul Thorndike. Family History. Negative. Previous History. Symptoms of gradually increasing obstruction two days before entrance, absolute constipation, vomiting.

May 23. Urine, normal; 1025; acid; slight possible trace of albumen; no sugar; no acetone; no diacetic acid.

Operation.—May 25, 1904. Ether. Dr. Paul Thorndike. Laparotomy. Carcinomatous mass found involving descending colon and sigmoid. Left inguinal colostomy.

June 15. Urine, slightly high; 1020; acid; no albumen; no sugar; acetone present; no diacetic acid. No clinical signs.

June 22. Urine negative. Normal convalescence.

CASE XXXIX.—*Appendicitis, Acute, with Abscess.*—J. C.; aged thirty years; married; driver. Admitted June 29, 1904. Service of Dr. F. S. Watson. Family History. Negative. Previous History. Negative.

Present Illness.—Sudden attack of cramp-like pain in abdomen yesterday morning. Vomited last night. Pain now localized in appendix region. Bowels constipated for past two days.

Physical Examination.—Looks sick. Odor of acetone to breath. Abdomen, scaphoid; marked muscular spasm on right side; great tenderness over region of appendix. Leucocytes, 25,000.

July 1. Urine, normal; 1030; acid; no albumen; no sugar. Acetone present; no diacetic acid.

Operation.—July 2, 1904. Ether. Dr. W. E. Faulkner. Appendix found to be gangrenous and was removed. Localized peritonitis. Drainage. Good recovery and convalescence. Pathological report, culture taken was sterile. Acute gangrenous appendix.

July 5. Urine negative; no further clinical signs; normal convalescence.

CASE XL.—*Fæcal Fistula.*—A. S.; aged forty years; female; baker. Admitted February 8, 1904, to Dr. H. W. Cushing's service.

Patient transferred from Medical Department, where she entered six days ago with history of steady vomiting for three weeks, associated with ingestion of food and slight epigastric pain and tenderness. Vomitus chiefly food material and containing no blood. Seven years ago had an abscess in right groin, which still discharges at intervals. Since entrance on medical service patient has had continual vomiting. Fed by nutrient enemata.

Physical Examination.—Well developed and nourished. Pupils equal and react to light. Tongue much reddened and dry. Throat reddened. No general glandular enlargement. Pulse equal, regular, fair volume, and tension. Heart, soft systolic at apex transmitted a short distance into axilla. Lungs negative. Reflexes normal. No œdema of extremities. Sweetish odor to breath. Abdomen, slight dulness in right side over an area the size of palm of hand; palpation reveals a rather soft, slightly irregular, apparently adherent mass which is slightly tender on pressure, about one-half inch above Poupart's ligament and one inch internal to anterior superior spine of right ileum. There is a sinus surrounded by an area the size of silver dollar of scar tissue. Probe introduced runs backward, slightly upward and outward, for a distance of about three inches. Pressure on mass in right side of abdomen causes flow of pus from sinus.

February 10. After transfer from Medical Service patient vomited several times after taking small amounts of water by mouth; then fed by nutrient enemata; and at the end of twenty-four hours, as no vomiting had ocurred and patient failed to retain two enemata, nourishment in the form of beef tea and Mellin's Food was given by mouth. Sweetish odor noticed on breath has continued to be present. Patient complains of feeling very drowsy, dry, and very weak; considerable photophobia and dimness of vision. Patient states that she has been menstruating for the past sixteen days. Considerable difficulty in obtaining specimen of urine. To-day about two ounces obtained, of which a satisfactory examination could not be made. Last night patient rejected several nutrient enemata. No vomiting has occurred except as above noted. Five loose bowel movements yesterday.

February 12. General condition about the same. Drowsiness, photophobia, and dimness of vision still continue. Tongue extremely red and dry. No urine passed yesterday. Catheterized and twelve ounces of urine obtained, which was amount secreted in past twenty hours. Patient again catheterized to-day, at end of twenty-four hours, and fourteen ounces of urine obtained. Examination of urine yesterday showed presence of acetone and diacetic acid.

February 12, 1904. Urine, twenty-four hours' amount, about 500 cubic centimetres. Color high; slightly turbid; 1020; acid; urea, 2.65 per cent. Indican present. Chlorides normal. No albumen. No sugar. No bile pigments. Acetone and diacetic acid present. Daily amount passed, eight to fourteen ounces. Starch enemata given yesterday and to-day for diarrhœa. On giving enema it was noticed that there was slight bubbling of gas and slight discharge of fluid from sinus above Poupart's ligament. Patient given yesterday thirty grains soda bicarbonate every two hours. Patient has retained all liquid nourishment by mouth until this morning, when she vomited about one ounce of semi-digested greenish, foul-smelling fluid. Eyes examined to-day by Dr. Allen Greenwood, who reports, " Examination of fundi shows nothing abnormal. Vessels appear normal as to size and color. Nerve heads normal. The partial loss of sight might be due to some disturbance in the postoccipital lobes such as occurs in the blindness of pregnancy without fundus changes. Possibly some toxic influence affecting the region of the brain mentioned."

February 15. Since last note patient has been semidelirious. Incontinence of fæces present past three days. Takes small amounts of liquid nourishment and complains of constant thirst. Fæcal discharge from sinus in right inguinal region. Sweetish odor still present in breath. Patient's general condition has slowly failed and, in spite of active stimulants, she died at 8.03 this morning. No autopsy.

CASE XLI.—*Gastric Dilatation (Gastro-enterostomy, Posterior)*.—R. M.; aged nineteen years; drug-clerk. Admitted May 18, 1904. Service of Dr. Abner Post.

Present Illness.—Indigestion past three years. Vomiting after meals past two months, one to two hours after eating. Transferred from medical service, where urine was not examined for acetone or diacetic acid. More or less vomiting during the past three months.

May 19. Urine, high; 1030; no albumen; no sugar. Acetone present; no diacetic acid; has vomited no blood.

Operation.—May 31, 1904. Ether. Dr. Paul Thorndike. Stomach and intestines found normal. Anterior gastro-enterostomy done. Good ether recovery.

June 1 and 2. Urine, high; 1032; no albumen; no sugar.

Acetone present; no diacetic acid. Vomiting continued after operation. Constant epigastric pain.

June 15. Condition same, drowsy, dull.

June 21. Failing steadily, vomiting continually. Odor of acetone to breath. Slightly delirious. Gradually failed; coma lasted four days, died June 24. No autopsy. Temperature subnormal two and a half weeks before death. Pulse-rate rose from 60 at time of operation steadily to 110 at time of death.

CASE XLII.—*Acute Alcoholism.*—R. H.; aged thirty-two years; female; married; housework. Admitted March 16, 1904. Service of Dr. G. G. Sears. Family History. Negative. Previous History. Negative.

Present Illness.—Debauch two weeks ago, has been vomiting night and day since. Has eaten no solid food since, but has continued drinking. Three days ago vomited blood. Dull, constant pain in epigastrium. Low eructation. Headache for past two days. Has had flashes of light before eyes. Passes urine once in twenty-four hours.

Physical Examination.—Well developed and nourished. Skin dry. Obese. Marked odor of acetone to breath. Tongue red and dry. Throat dry. Heart and lungs normal. Liver-dulness normal. Slight epigastric tenderness. Vomiting lasted three days following entrance.

March 16. Urine, normal color; 1025; neutral; slight trace of albumen; no sugar. Acetone and diacetic acid present. Amount passed in twenty-four hours averaged during ten days from ten to twenty-two ounces.

March 20. Takes food readily now. Acetone odor has disappeared. Examination of urine negative. Good convalescence.

CASE XLIII.—*Burns; Typhoid Fever.*—B. P.; aged sixteen years; female; no occupation. Admitted December 21, 1903. Service of Dr. F. S. Watson.

Previous History.—Epileptic attacks since age of two. No attacks from ten to fifteen years of age. Since then irregularly until past three weeks, when they have occurred every other day.

Present Illness.—Two days before entrance, patient during an epileptic attack fell on an oil-stove, sustaining burns of both arms and chin.

Physical Examination.—Excessive sloughs of both forearms.

Considerable swelling, redness, and tenderness of inside of both arms. Glands in axillæ.

December 22. Urine negative.

December 29. Wounds granulating.

January 11, 1904. Wounds granulating fairly well. Heart's action rapid. Temperature elevated. Patient complains at times of abdominal pain relieved by enemata. General condition fair.

January 18. Burns doing well. For several days has complained of abdominal pain and vomiting. Has not taken food well. The possibility of intestinal ulcer is considered and patient is put on rectal feeding. Considerable tenderness in epigastrium. Very pale. Pulse weak and rapid, and patient apparently failing.

January 25. Patient is failing. After being kept on rectal feeding for one week, has been given small amounts of liquid by mouth, but vomits everything. Burnt areas healing slowly. Patient seen in consultation by Dr. H. S. Burrell, at whose suggestion urine was examined for acetone, which was present in large amount. Odor to breath. Patient very stupid, dull, and drowsy. Given solution of bicarbonate of soda subpectorally, later also added to nutrients. Patient continued to vomit and died. Widal negative. Leucocytes, 10,200.

Autopsy January 26, 1904. Body, Dr. Mallory; head, Dr. Southard. Autopsy, twenty-one hours' post-mortem. Aged sixteen years. Body length, 160 centimetres.

Fairly well developed, very poorly nourished white female. Slight lividity of dependent portions and slight rigor mortis. Œdema noted in tissue of chest on section, not noticeable in extremities due to salt infusion. Pupils equal. Rather extensive granulating superficial wounds of each forearm.

Peritoneal Cavity.—Contains 400 cubic centimetres of straw-colored fluid slightly clouded with small flakes of fibrin. Intestine grayish, smooth, and shining; show many dark-red, firm areas in lower portions of ileum, most marked at ileocæcal valve. Mesenteric lymph-nodes are large (two centimetres diameter and less), of dark-red color and firm. On section, cut surface is of uniform grayish pink with pin-head, whitish areas scattered over it.

Pleural Cavity.—Not remarkable. *Pericardial Cavity.*—Contains thirty cubic centimetres of clear straw-colored fluid. *Heart Weight*, 190 grammes. Subepicardial fat in small amount. *Myo-*

cardium dark red and firm, shows in fresh section (Scharlach R. stain), no fat. *Endocardium* and *valves* normal. Coronary arteries not remarkable.

Measurements.—Tricuspid valve, 11 centimetres; pulmonary valve, 6 centimetres; mitral valve, 8 centimetres; aortic valve, 5.5 centimetres; left ventricle, 1.5 centimetres; right ventricle, 0.5 centimetre.

Lungs.—Of delicate pink color anteriorly, dark blue at back, crepitate throughout. On section not remarkable.

Spleen Weight, 245 grammes. Capsule tense. Substance dark red and firm. Trabeculæ and Malpighian bodies visible.

Gastro-intestinal Tract.—Peyer's patches in lower 150 centimetres of ileum appear as dark red, firm, slightly elevated areas with long axis in direction of intestinal lumen. Some of these just above ileocæcal valve show small yellowish sloughs still attached to surface. Other patches show small ragged superficial ulcerations. *Pancreas* appears normal. *Liver Weight,* 1640 grammes. On section, cut surface is of brownish-red color, paler than usual, and rather friable. No focal lesions seen. Central veins empty. Fresh section (Scharlach R. stain) shows very slight amount of fat in peripheries of lobules.

Kidney Weight, 295 grammes. Capsule strips readily, leaving smooth surface. Cortex of light grayish color, fairly firm, is distinctly marked off from dark-red pyramids, and shows glomeruli as fine, glistening, pinpoint elevations. Fresh section (Scharlach R. stain) shows no fat.

Adrenals appear normal. *Bladder,* genital organs, and aorta appear normal.

Head.—Hair thick, dark. Scalp normal. Cranium thin, without diploë. Dura adherent to calvarium under bregma. Sinuses contain fluid blood. Villi slightly developed. Pia bags out loosely, containing considerable clear fluid, which can be moved about readily between gyri. A few fibrous streaks and thickenings in pia alongside veins, notably in Sylvian fossæ. Gyri not œdematous, strike one at first as narrowed, but prove normal on section. Puncta crumenta distinct in medullary portion of substance. Ventricles contain a slight surplus of clear fluid. Ependyma of floor of lateral ventricles has a rather coarse, salt-sprinkled appearance. Interbrain, isthmus, and cerebellum normal.

Middle Ears.—Normal.

Anatomical Diagnoses.—Chronic external pachymeningitis; chronic fibrous leptomeningitis; œdema of pia; moderate chronic internal hydrocephalus; chronic ependymitis; lesions of typhoid fever; acute splenitis; hyperplasia of mesenteric lymph-nodes; hyperplasia of Peyer's patches with necrosis; ascites; fatty liver.

CASE XLIV.—*Fracture of Shaft of Femur.*—H. S.; aged six years; school-boy. Admitted October 26, 1903. Service of Dr. W. P. Bolles. Family History. Negative. Previous History. Negative.

Present Illness.—Patient fell from back of team, catching leg in wheel, receiving lacerated wound just below knee and transverse fracture of middle shaft of femur.

October 23, 1903. Operation. Ether. Dr. Kelly. Repair, suture of wound. Plaster-of-Paris spica.

December 10. Ether given again on account of malposition of fragments, union broken up and apparatus (extension) applied.

February 25. Convalescence. All apparatus off. Patient up.

February 29, 1904. Three days ago patient vomited several times, and had slight puffiness of face. Urine became smoky and showed microscopical blood.

February 28. Urine, smoky; 1030; acid; albumen, one-eighth of 1 per cent.; no sugar. Acetone and diacetic acid present. Normal and abnormal blood. No casts or renal cells seen. Next day patient somewhat improved. Not so well to-day and has vomited considerably. Some headache. Acetone odor to breath. Two days ago acetone and diacetic acid present in urine. Some puffiness of face.

March 1. Acetone and diacetic acid present in urine; no blood; no albumen.

March 3. Acetone and diacetic acid absent from urine. No vomiting past three days. Patient much brighter. No puffiness of face. Soda bicarbonate, xxx grains, every three hours, for past six days. Normal convalescence.

March 19. Discharged relieved.

CASE XLV.—*Hæmorrhoids.*—D. B.; aged thirty-four years, female; married; housework. Admitted July 8, 1904. Service of Dr. G. H. Monks.

Present Illness.—Discomfort in region of anus for past twelve years. Piles protruded past year on defecation, with pain.

Local Examination.—Several hæmorrhoidal masses about rectum. No ulceration.

July 9. Urine, normal; 1024; acid; no albumen; no sugar; no acetone; no diacetic acid.

July 11, 1904. Operation. Ether. Dr. Kelly. Hæmorrhoidal masses excised and edges sutured with chromicized catgut No. 2.

July 12. Urine passed, normal; 1017; acid; no albumen; no sugar; acetone present; no diacetic acid. No clinical symptoms excepting slight odor of acetone to breath. No further examination made of urine. Normal convalescence.

CASE XLVI.—*Appendicitis, Acute, with Abscess.*—J. H., aged six years; school-girl. Admitted July 10, 1904. Service of Dr. G. H Monks Family History. Negative. Previous History. Negative.

Present Illness.—Four days ago pain in abdomen localized in right side over area the size of palm of hand, just beneath liver extending into lumbar region. Vomiting; odor of acetone to breath. Leucocytes, 14,400. Slight dulness over above area, tenderness and marked muscular spasm.

July 10, 1904. Operation. Ether. Dr. G. H. Monks. Appendix, abscess found just beneath liver. Appendix running up and behind cæcum and retroperitoneally. Appendix gangrenous and perforated; removed. Good ether recovery. Urine passed the day of operation, normal; 1025; no albumen; no sugar; acid. Acetone and diacetic acid present.

July 13. Urine, negative. Patient doing well. No vomiting following operation. Patient slightly dull, otherwise no symptoms. Normal convalescence.

CONCLUSION.

In presenting this series of cases, it is not my intention to attempt to formulate some definite theory for the causation of the condition present. I simply wish to present a series of cases which I feel sure are identical with those reported by other observers.

At present our knowledge of the conditions accountable for the symptoms present, and for the occurrence of acetone and diacetic in the urine, is yet in its infancy. It has been proved experimentally that it is not due to acetone circulating in the blood, as the same condition has been produced experimentally by other substances. The amount of acetone found in the urine is no index as to the severity of the affection. Whether the occurrence of the symptoms is due to a toxic substance acting on psychomotor centres, or due to pressure on these centres, has not been proven. This is only offered as a suggestion as to the causation. That there is some toxæmia occurring is doubtless true; whether it is due to the presence of volatile fatty acids, to the rapid destruction of proteid matter, or to the rapid elimination of the alkalies is impossible to say at the present time.

The object of this paper is to report a series of cases in which the condition has been present in a large proportion; to call attention to the condition as it exists in surgical cases; to show that what has been considered as a rather fatal condition is present mildly in a variety of cases, and to hope that it will stimulate to some extent experimental and clinical investigation.

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